REMARKS

Claims 28-42, 44-46 and 48-50 are presently pending. Support for amendments to Claim 28 and 44-46 are found in the Specification as filed, for example at paragraphs [0013] and [0030]. Claims 43 and 47 are canceled without prejudice. Support for new Claim 50 is found in the Specification as filed at paragraph [0013]. No new matter has been added herewith. The following addresses the substance of the Office Action.

Indefiniteness

Claims 28-49 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claim 1 recited the term "unspecified binding" in line 1 and Claim 29 recited "non-specific antibody binding" in line 2. However, the specification does not define these terms. Applicants have amended Claim 28 to remove recitation of "unspecific binding".

Claims 28 and 43 recited the term "disturbing effects of matrices" at line 2 but there is no definition of the term in the Specification. Applicants have amended Claim 28 to remove recitation of "disturbing effects of matrices" and Claim 43 is canceled.

In Claim 37, the valency of the carbon attached to the OH group in the substitution group -[O-CH_2-CH_3]-OH was incorrect. Applicants have replaced the second instance of "CH_3" with --CH_2--.

Anticipation

Salonen

Claims 28, 32, 34-39, 42-43 and 47-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by Salonen (GB 2062224A). The Examiner noted that Salonen discloses an immunoassay method that comprises reaction of a binding pair member in a solution comprising phosphate buffer, polyethylene glycol (i.e., Compound A), a non-ionic detergent (e.g., Tween 20) and NaCl. Salonen discloses that polymers such as polyethylene glycol exert a promoting effect on the interaction between soluble antigens and antibodies, apparently by steric exclusion of the immune complexes from the domain of the polymer. Thus, the method of Salonen accelerates immunological antigen-antibody reactions. The Examiner concluded that, since the reaction mixture of Salonen comprises the same reaction components as in the presently claimed methods, it would inherently reduce unspecific binding.

Applicants have amended Claim 28 by removing recitation of "reducing unspecific binding and/or cross-reactivity and/or disturbing effects of matrices" and by adding recitation of a method of detecting presence or amount of a first member of a binding pair in a sample from a patient known or suspected of containing heterophilic antibodies, the method comprising conducting a specific binding reaction comprising binding of the first member of the binding pair with a second member complementary member of the binding pair in an aqueous solution as defined in the present claims, thereby reducing an influence of heterophilic antibodies present in the sample on the specific binding reaction of the binding pair.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed.Cir. 1986). "[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). Since Salonen et al. does not disclose a method of reducing an influence of heterophilic antibodies present in the sample on the specific binding reaction of a binding pair, the reference does not anticipate the claimed methods. Accordingly, the Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Figard

Claims 28, 32, 34-38, 42-43 and 47-48 were rejected under 35 U.S.C. § 102(b) as being unpatentable over Figard (U.S. Patent No. 5,616,460). The Examiner noted that Figard discloses an aqueous composition suitable for use as a buffer in an immunoassay method, wherein the composition comprises a biological buffer, ethylene glycol and a detergent. Figard discloses at column 2, lines 53-63 that the composition is particularly useful for stabilizing the immunoreactivity of antigens. However, Figard does not disclose a method of reducing an influence of heterophilic antibodies present in a sample on the specific binding reaction of a binding pair.

As discussed above, anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. Thus, Figard does not anticipate the claimed methods and the Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Siedel et al.

Claims 28, 29, 30, 32, 34-38, 41-43 and 47-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by Siedel et al. (U.S. Patent No. 4,485,177). The Examiner pointed out that Siedel et al. teaches a reagent suitable for use in an immunoassay method, wherein the reagent comprises a buffer, a non-ionic detergent and polyethylene glycol. However, Siedel et al. does not disclose a method of reducing an influence of heterophilic antibodies present in a sample on the specific binding reaction of a binding pair.

As discussed above, anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. Thus, Siedel et al. does not anticipate the claimed methods and the Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Stewart et al.

Claims 28-38, 41-43 and 47-48 were rejected under 35 U.S.C. § 102(b) as being anticipated by Stewart (U.S. Patent No. 6,503,702). The Examiner noted that Stewart teaches an immunoassay buffer system comprising a buffer, a detergent, a salt, a stabilizing agent and a protein, wherein the stabilizing agent can be polyethylene glycol. Stewart developed a versatile buffer system that balances the strength required of an extraction method with the delicacy required for antibody-antigen binding. However, Stewart does not disclose a method of reducing an influence of heterophilic antibodies present in a sample on the specific binding reaction of a binding pair.

As discussed above, anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. Thus, Stewart does not anticipate the claimed methods and the Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Obviousness

Claims 33 40 and 49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Salonen (*supra*). In addition, Claims 33, 39, 40, 44-46 and 49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Figard (*supra*). Claims 31, 33, 39, 40, 44-46 and 49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Siedel et al. (*supra*). Finally,

Claims 39-40, 44-46 and 49 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Stewart (*supra*). The claims were rejected over the cited references because the Examiner concluded that the subject matter claimed was merely a matter of judicious selection and routine optimization of conditions, which is well within the purview of the skilled artisan.

Referring to the Specification as filed at paragraph [0013], the Applicants discovered that an undesirable influence of heterophilic antibodies during a specific binding reaction of a binding pair can be prevented when an aqueous solution according to the present invention is used. These results were unexpected because, based on the prior art, one of ordinary skill in the art would have had no way of knowing that heterophilic antibody binding during a specific binding reaction of a binding pair could be reduced by the presently claimed method.

Referring to the Rule 132 Declaration by Dr. Peter Rauch submitted herewith, the Applicants conducted experiments, which show that an undesirable influence of heterophilic, human anti-mouse antibodies (HAMA) during a specific binding reaction is unexpectedly reduced by using the presently defined aqueous solution. The HAMA effect is depicted schematically in Figure 1. As illustrated, HAMA can cross-link capture antibody and labeled detecting antibody, resulting in a false positive signal (panel B). Alternatively, HAMA may bind to capture antibody or detecting antibody resulting in a false negative signal (panels C and D). Figures 2-4 demonstrate a reduction of the HAMA effect when the sample buffer of the presently claimed method was utilized. The reduction of the HAMA effect on the specific binding reaction of a binding pair was unexpected since, based on the prior art of record, one of ordinary skill in the art would have had no way of knowing that an influence of heterophilic antibodies on the specific binding reaction of a binding pair could be reduced by the presently claimed method.

In view of the amendments to the claims and the preceding remarks, the Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other

broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: December 8, 2009

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